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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/443,070 11/18/99 GILTON

T 3530.2US

EXAMINER

HM22/0626

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ART UNIT	PAPER NUMBER

1641

14

DATE MAILED:

06/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.

09/443,070

Examiner

Gailene R. Gabel

Applicant(s)

GILTON, TERRY L.

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 30 May 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check only a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.
3. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search. (see NOTE below);
 - (b) ☐ they raise the issue of new matter. (see Note below);
 - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

4. ☐ Applicant's reply has overcome the following rejection(s): _____.
5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
6. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):
- Claim(s) allowed: NONE.
- Claim(s) objected to: NONE.
- Claim(s) rejected: 1, 2, 8 and 12-31.
- Claim(s) withdrawn from consideration: NONE.
9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.
10. ☒ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). 13.
11. ☐ Other:

Continuation of 6. does NOT place the application in condition for allowance because: Applicant's arguments have been previously addressed in Paper No. 11 and are not persuasive. Also, the pending claims to date fail to obviate the prior art of record.

DETAILED ACTION

Amendment Entry

1. Applicant's response filed 3/30/01 in Paper No. 12 is acknowledged. Claims 1-2, 8, and 12-31 are pending.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-2, 8, and 12-31 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reason of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-2, 8, 14-16, 18-20, 22-23, and 26-28 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Isaka et al. (US 5,482,598) for reason of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 12-13, 21, 24-25, and new claims 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isaka et al. (US 5,482,598) in view of Sunzeri (US 5,536,382) and Swedberg et al. (US 5,571,410) for reason of record.
5. Claims 17 and 29 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Isaka et al. (US 5,482,598) in view of Northrup et al. (US 5,882,496) for reason of record.

Response to Arguments

6. A) Applicant contends that the specification provides support for the recitation of "a matrix including the same material as a nonporous substrate" and finds support in page 8, line 20 (24-25) and page 7, lines 11-13 (14-16) of the specification.

In response, page 8, lines 20, 24-25 encompasses "a porous silicon with a silicon substrate". Page 7, lines 14-16, likewise, encompasses "a porous silicon or HGS formed on a silicon substrate". Specifically, the limitation recited in claims 1 and 18 define that the "the matrix of the porous capillary column may be formed from the same

material as the nonporous substrate” and is therefore not fully supported and encompassed by the specification.

B) Applicant argues that Isaka does not anticipate the claimed invention because claim 1 recites a separation method that includes applying a sample to an end of a porous capillary column that includes a matrix and at least one capture substrate disposed thereon so that a constituent may be separated from the sample. Applicant further argues that Isaka merely discloses the and exemplifies use of enzymes: uricase and invertase, which couple to a substrate, to catalyze a reaction; thus a chemical change, to the substrate resulting to a detectable change or a measurable detection product. Applicant further argues that Isaka does not disclose that the measurable product is “separated” from the remainder but rather exits the outlet port with the remainder of the sample.

In response, Isaka indeed, reads on what is recited by the claimed invention because the same basic elements and mechanism of “capturing, isolating, and detecting a constituent from a sample” is taught in Isaka wherein the porous matrix functions as a filter to enhance separation of the desired constituent from the sample (see column 4, lines 16-27) and wherein the porous matrix may include a capture substrate, in this case an **immobilized** enzyme, to effect separation based on the affinity of the constituent with the capture substrate. In column 3, lines 10-11, Isaka specifically discloses that “uricase is immobilized in the porous channel to check (by capturing and detecting) the amount of uric acid in serum” in the sample- and the

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constituent (uric acid) is separated by "capture" of the uric acid analyte by the affinity species (uricase) in the matrix, then the reaction product is detected. Further, the rejected claims do not exclude that the measurable product exits the outlet port of the capillary column with the remainder of the sample but rather only that the capillary column "enhances separation of the constituent from the sample by said at least one capture substrate".

C) Applicant argues that Isaka does not disclose that the stationary phase is disposed on a selected location along the capillary column.

In response, "selected location" of a stationary phase containing a capture substrate in a capillary column constitutes a result effective variable which the prior art references have shown may be altered in order to achieve optimum results. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges, i.e. a selected location, by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). Alternatively, selected locations for use as stationary phase in a capillary column constitute an obvious design choice by the Applicant which is obtained by normal optimization procedures.

D) Applicant argues that a prima facie case of obviousness has not been established in the combined prior art references cited because there is no motivation to combine the teachings of Sunzeri and Swedberg with Isaka because 1) the specific

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binding partner in Sunzeri is not immobilized to the capillary substrate, but rather the binding elements are prebound, and therefore one of ordinary skill in the art would not be motivated by the teachings or suggestions of Sunzeri to immobilize a specific binding partner to capture the other member, and 2) Swedberg teaches a capillary electrophoresis separation device which includes an open trench formed in a substrate filled with different synthetic porous materials; therefore, one of ordinary skill in the art would not have been motivated to apply the teachings of Swedberg to the subject matter of Isaka.

In response, obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the rejection is based on the combined teachings of the references as follows. Isaka discloses a method of isolating constituents in a sample using a chromatography apparatus wherein the sample is applied to a first end of the capillary matrix then drawn across a flowfront through the porous matrix channel from the second end by capillary action or, otherwise, by differential pressure. The porous matrix functions as a filter which enhances separation

of the desired constituent from the sample and may include a capture substrate wherein separation is on the basis of affinity or absorptivity of the constituent with the capture substrate in a reaction. Sunzeri is incorporated only for his teaching of the benefit of including internal and external standards or controls alongside sample analysis in capillary electrophoresis. Swedberg is incorporated for his teaching of a stationary phase in miniaturized column devices onto which separation and capture functions are combined in the matrix, i.e., **affinity chromatography** matrix which specifically includes a variation of selected biological affiants: an antibody, an antigen, a lectin, enzyme etc. to function as the capture species.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the capture substrate in the chromatographic separation apparatus taught by Isaka to include other capture species such as antigens and antibodies, such as taught in the affinity chromatographic matrix of Swedberg in order to achieve enhanced simultaneous performance of separation, filtration, and capture function in a single chromatographic device because Swedberg specifically suggested that a variation of capture species can be incorporated into separation devices to perform such capture function.

One of ordinary skill in the art would have been motivated to combine the teachings of Swedberg in incorporating a variation of species into a separation matrix with teaching of Isaka in using porous silicon matrix in a capillary column for separation because Isaka specifically taught the advantage of porous silicon as matrix because of its established porosity which enhances capacity for separation, augments adsorption,

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differentiates flow rate in samples, thereby producing a highly versatile miniaturized chromatographic device capable of enhanced partitioning and complexation reactions. Furthermore, with the advent of silicon micromachining and LIGA in the teachings of Swedberg, one of ordinary skill in the art would have reasonable expectation of success in fabricating multiple separation columns or channels with a high degree of uniformity and precision in order to allow side by side accurate comparative and correlative measurement of sample results in comparison to internal controls, references, or standards with known measurement levels such as taught by Sunzeri, because quality control monitoring is standard laboratory practice and a well known art for monitoring the functionality, accuracy, and precision of various laboratory apparatus and methods. It must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

7. Applicant's arguments filed 3/30/01 have been fully considered but they are not persuasive. Accordingly, no claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703)

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305-0807. The examiner can normally be reached on Monday to Thursday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

 6/19/01

Gailene R. Gabel
Patent Examiner
Art Unit 1641


CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800/1641